

REMARKS

Claims 1-15 and 29-40 are pending in this application. It is respectfully requested that this amendment amending claims 2, 14, 15, 29, 32, 36, 39 and 40 and adding claims 41-45 be entered into this application.

Claim 2 has been amended to correct the case of $\text{SO}_2(\text{C}_1\text{-C}_6 \text{ alkyl})$.

Claim 14 has been amended to delete the phrases “such as fibromyalgia” and “including cerebral ischemia” and to add “excitotoxic neuronal damage.” Support for the addition of “excitotoxic neuronal damage” in claim 14 is found on page 25, line 18 of the specification.

New claim 41 depends from claim 14 and defines the pain perception as fibromyalgia.

New claim 42 depends from claim 14 and defines the ischemic neuronal damage as cerebral ischemia.

Claim 15 has been amended to delete the phrase “such as depression and postpartum depression”.

New claim 43 depends from claim 15 and defines the mood disorders as depression or postpartum depression.

New claim 44 depends from claim 15 and defines the ischemic neuronal damage as cerebral ischemia.

New claim 45 depends from claim 15 and defines the mammal as a human.

Claim 29 has been amended to replace “R24 and R25” with “ R_{24} and R_{25} ”.

Claim 32 has been amended to insert - - and - - between “depression” and “child”.

Claim 36 has been amended to delete the word “including” in line 2 of the claim.

Claim 39 has been amended to depend from claim 42.

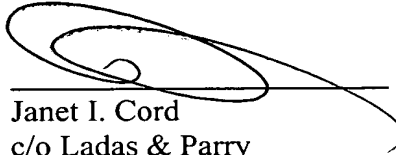
Claim 40 has been amended to place a period at the end of the claim.

In view of these amendments, it is respectfully requested that the objections to claims

2, 14, 15, and 29 and the rejection of claims 14, 15, 36 and 40 under 35 USC 112, second paragraph included in the Official Action of April 17, 2003 be withdrawn.

Accordingly applicants submit that the present application is in condition for allowance.

Respectfully submitted,

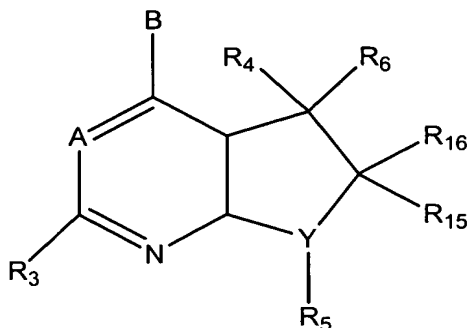
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In the Claims

2.(Twice Amended) A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is $-\text{CR}_7$ or N;

B is $-\text{NR}_1\text{R}_2$, $-\text{CR}_1\text{R}_2\text{R}_{11}$, $-\text{C}(=\text{CR}_2\text{R}_{12})\text{R}_1$, $-\text{NHCHR}_1\text{R}_2$, $-\text{OCHR}_1\text{R}_2$, $-\text{SCHR}_1\text{R}_2$, $-\text{CHR}_2\text{OR}_{12}$, $-\text{CHR}_2\text{SR}_{12}$, $-\text{C}(\text{S})\text{R}_2$ or $-\text{C}(\text{O})\text{R}_2$;

Y is $-\text{CH}$ or N;

R_1 is C_1 - C_6 hydrocarbyl which may optionally be substituted with one or two substituents R_8 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF_3 , C_1 - C_4 alkoxy, $-\text{O}-\text{CO}-(\text{C}_1$ - C_4 hydrocarbyl), $-\text{O}-\text{CO}-\text{NH}(\text{C}_1$ - C_4 hydrocarbyl), $-\text{O}-\text{CO}-\text{N}(\text{C}_1$ - C_4 hydrocarbyl)(C_1 - C_2 hydrocarbyl), $-\text{NH}(\text{C}_1$ - C_4 hydrocarbyl), $-\text{N}(\text{C}_1$ - C_2 alkyl)(C_1 - C_4 hydrocarbyl), $-\text{S}(\text{C}_1$ - C_4 alkyl), $-\text{N}(\text{C}_1$ - C_4) $\text{CO}(\text{C}_1$ - C_4 hydrocarbyl), $-\text{NHCO}(\text{C}_1$ - C_4 hydrocarbyl), $-\text{COO}(\text{C}_1$ - C_4 hydrocarbyl)hydrocarbyl, $-\text{CONH}(\text{C}_1$ - C_4 hydrocarbyl), $-\text{CON}(\text{C}_1$ - C_4 hydrocarbyl)(C_1 - C_2 alkyl), CN , NO_2 , $-\text{SO}(\text{C}_1$ - C_4 hydrocarbyl) and $-\text{SO}_2(\text{C}_1$ - C_4 hydrocarbyl), and wherein said C_1 - C_6 hydrocarbyl and the (C_1 - C_4)hydrocarbyl moieties in the foregoing R_1 groups may optionally contain one carbon-carbon double or triple bond;

R_2 is C_1 - C_{12} hydrocarbyl, aryl or $-(\text{C}_1$ - C_4 hydrocarbylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or $-(\text{C}_1$ - C_6 alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said $-(\text{C}_1$ - C_6 alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by $\text{N}-\text{R}_9$, wherein R_9 is hydrogen or C_1 - C_4 alkyl; and wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and C_1 - C_4 alkyl, or with one substituent selected from bromo, iodo, C_1 - C_6 alkoxy,

-O-CO-(C₁-C₆ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), CN, NO₂, -SO(C₁-C₄ alkyl), and -SO₂(C₁-C₄ alkyl), and wherein said C₁-C₁₂ hydrocarbyland the C₁-C₄ hydrocarboylene moiety of said -(C₁-C₄ hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR₁R₂ or -CR₁R₂R₁₁ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, methylthio, methylsulfonyl, CH₂OH, or CH₂OCH₃;

R₄ is hydrogen, C₁-C₄ hydrocarbyl, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, trifluoromethoxy, -CH₂OCH₃, -CH₂OCH₂CH₃, -CH₂CH₂OCH₃, -CH₂OF₃, CF₃, amino, nitro, -NH(C₁-C₄ alkyl), -N(CH₃)₂, -NHCOCH₃, -NHCONHCH₃, -SO_n(C₁-C₄ hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C₁-C₄ hydrocarbyl), -CHO, cyano or -COO(C₁-C₄ alkyl) wherein said C₁-C₄ hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substituent selected from hydroxy, amino, -NHCOCH₃, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)₂, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, chloro, cyano and nitro;

R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R₅ is substituted with from one to three substituents independently selected from fluoro, chloro, C₁-C₆ alkyl, and C₁-C₆ alkoxy, or with one substituent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C₁-C₆ alkyl)O(C₁-C₆)alkyl, -NHCH₃, -N(CH₃)₂, -COOH, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and [-SO₂(C₁-C₆ alkyl)] -SO₂(C₁-C₆ alkyl), and wherein the C₁-C₄ alkyl and C₁-C₆ alkyl moieties of the foregoing R₅ groups may optionally be substituted with one or two fluoro groups or with one substituent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R₆ is hydrogen or C₁-C₆ alkyl, wherein C₁-C₆ alkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

R₇ is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, -O(C₁-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -OCF₃, CF₃, -CH₂OH, -CH₂OCH₃ or -CH₂OCH₂CH₃;

R₁₁ is hydrogen, hydroxy, fluoro, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl; and

R₁₆ and R₁₇ are each independently, hydrogen, hydroxy, ethyl, ethyl, methoxy, or ethoxy, except that R₁₆ and R₁₇ are not both methoxy or ethoxy;

or R₁₆ and R₁₇ together form an oxo (=O) group;

or a pharmaceutically acceptable salt of such compound.

Claim 14 (Twice Amended) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF or (b) a disorder or condition selected from inflammatory disorders, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception [such as fibromyalgia]; mood disorders, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases, gastrointestinal diseases; eating disorder; hemorrhagic stress; chemical dependencies or addictions; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage[,]; excitotoxic neuronal damage; [including cerebral ischemia;] epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

Claim 15 (Twice Amended). A pharmaceutical composition according to claim 14 for the treatment of a disorder selected from inflammatory disorders; pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders [such as depression,, and postpartum depression]; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases; gastrointestinal diseases; eating disorders; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal[, including a human].

Claim 29 (Amended). A compound as claimed in claim 1 wherein [R24 and R25] R₂₄ and R₂₅ are selected from- CF_3 , $-\text{CHF}_2$, CF_2CF_3 , and CH_2CF_3 [,].

Claim 32 (Amended). A pharmaceutical composition as claimed in claim 14 for

treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, and child abuse induced depression.

Claim 36 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of stress induced immune dysfunctions selected from the group consisting of [including] porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.

Claim 39 (Amended). A pharmaceutical composition as claimed in claim [14] 42 wherein the [for treatment of] cerebral ischemia [, selected from the group consisting of] is cerebral hippocampal ischemia[; excitotoxic neuronal damage].

Claim 40 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of social phobia, agoraphobia, and specific phobias.